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(54) **GP2 isoforms and their use in autoantibody capture**

(57) The invention relates to a method for binding or capturing autoantibodies directed to various Glycoprotein 2 (GP2) isoforms. In particular the invention provides an in vitro method for the diagnosis of an autoimmune disorder by the detection of autoantibodies that bind one or more isoforms of GP2. The invention is characterised by the provision of multiple isoforms of GP2 as autoantibody targets and encompasses the practical utilisation of the finding that the isoform specificity of anti-GP2 au-

toantibodies enables determination of particular autoimmune diseases. The invention also provides a kit developed for carrying out the claimed method. The present invention is useful for determining whether a sample from an individual comprises autoantibodies associated with an autoimmune disease, and for differentiating between multiple autoimmune diseases that exhibit similar symptoms, such as Celiac disease (CeD), Crohn's disease (CD) and/or ulcerative colitis (UC).

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## EUROPEAN SEARCH REPORT

Application Number  
EP 15 15 6756

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DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (IPC)
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X	WO 2011/130546 A1 (INOVA DIAGNOSTICS INC [US]; NORMAN GARY L [US]; SHUMS ZAKERA [US]) 20 October 2011 (2011-10-20) * claims 9-10, 13-16, figures 1 and 2 *	1-4, 7	
X	WO 96/17873 A1 (ALPHAGENE INC [US]) 13 June 1996 (1996-06-13) * claims 53-54, 56-59; *	10-15	
X	Dirk Roggenbuck ET AL: "Crohn's disease specific pancreatic antibodies: clinical and pathophysiological challenges", Clin Chem Lab Med, 14 November 2013 (2013-11-14), pages 483-494, XP055130857, DOI: 10.1515/cclm-2013-0801 Retrieved from the Internet: URL: <a href="http://www.degruyter.com/view/j/cclm.2014.52.issue-4/cclm-2013-0801/cclm-2013-0801.xml">http://www.degruyter.com/view/j/cclm.2014.52.issue-4/cclm-2013-0801/cclm-2013-0801.xml</a> [retrieved on 2014-07-22] * abstract, table 1, page 485, right-hand column, paragraph 1, page 486, left-hand column, paragraph 2, page 488, right-hand column paragraph 2 through page 489, right-hand column paragraph 2; *	1-5, 7, 9-15	
			TECHNICAL FIELDS SEARCHED (IPC)
			G01N
<p><del>The present search report has been drawn up for all claims</del></p>			
Place of search		Date of completion of the search	Examiner
Munich		17 September 2015	Pilch, Bartosz
<p>CATEGORY OF CITED DOCUMENTS</p> <p>X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document</p> <p>T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons &amp; : member of the same patent family, corresponding document</p>			

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DOCUMENTS CONSIDERED TO BE RELEVANT			
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X	DIMITRIOS P BOGDANOS ET AL: "Pancreatic-specific autoantibodies to glycoprotein 2 mirror disease location and behaviour in younger patients with Crohn's disease", BMC GASTROENTEROLOGY, vol. 12, no. 1, 1 January 2012 (2012-01-01), pages 102-102, XP055130943, ISSN: 1471-230X, DOI: 10.1186/ar2949 * abstract, page 3, left-hand column, paragraph 2, right-hand column, last paragraph through page 4, left-hand column paragraph 1, tables 2-4, page 6, left-hand column, paragraph 1 through page 8, left-hand column paragraph 4; *	1-4,7, 10-15	TECHNICAL FIELDS SEARCHED (IPC)
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The present search report has been drawn up for all claims			
Place of search Munich		Date of completion of the search 17 September 2015	Examiner Pilch, Bartosz
CATEGORY OF CITED DOCUMENTS X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document		T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons ..... & : member of the same patent family, corresponding document	

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DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (IPC)
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X	VALLORANI M ET AL: "P280 Anti glycoprotein-2 antibody in pediatric inflammatory bowel disease and celiac disease: prevalence, diagnostic value and variation at follow-up", JOURNAL OF CROHN'S AND COLITIS, vol. 8, 20 February 2014 (2014-02-20), XP028617533, ISSN: 1873-9946, DOI: 10.1016/S1873-9946(14)60401-3 * Abstract P280 *	1-5,7, 9-15	
X	BONACI-NIKOLIC BRANKA ET AL: "Autoantibodies to GP2, the major zymogen granule membrane glycoprotein, in patients with gluten-sensitive enteropathy: A possible serological trap", CLINICA CHIMICA ACTA, ELSEVIER BV, AMSTERDAM, NL, vol. 413, no. 7, 16 January 2012 (2012-01-16), pages 822-823, XP028902407, ISSN: 0009-8981, DOI: 10.1016/J.CCA.2012.01.005 * the whole document *	1-5,7, 9-15	
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The present search report has been drawn up for all claims			
Place of search Munich		Date of completion of the search 17 September 2015	Examiner Pilch, Bartosz
<p>CATEGORY OF CITED DOCUMENTS</p> <p>X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document</p> <p>T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons &amp; : member of the same patent family, corresponding document</p>			

EPO FORM 1503 03.82 (P04C01)



Application Number

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**CLAIMS INCURRING FEES**

The present European patent application comprised at the time of filing claims for which payment was due.

☐ Only part of the claims have been paid within the prescribed time limit. The present European search report has been drawn up for those claims for which no payment was due and for those claims for which claims fees have been paid, namely claim(s):

☐ No claims fees have been paid within the prescribed time limit. The present European search report has been drawn up for those claims for which no payment was due.

**LACK OF UNITY OF INVENTION**

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

see sheet B

☐ All further search fees have been paid within the fixed time limit. The present European search report has been drawn up for all claims.

☐ As all searchable claims could be searched without effort justifying an additional fee, the Search Division did not invite payment of any additional fee.

☒ Only part of the further search fees have been paid within the fixed time limit. The present European search report has been drawn up for those parts of the European patent application which relate to the inventions in respect of which search fees have been paid, namely claims:

1-5(completely); 7, 9-15(partially)

☐ None of the further search fees have been paid within the fixed time limit. The present European search report has been drawn up for those parts of the European patent application which relate to the invention first mentioned in the claims, namely claims:

☐ The present supplementary European search report has been drawn up for those parts of the European patent application which relate to the invention first mentioned in the claims (Rule 164 (1) EPC).



**LACK OF UNITY OF INVENTION  
SHEET B**

Application Number

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The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

1. claims: 1-4(completely); 7, 10-15(partially)

In vitro method for the diagnosis of an autoimmune disorder by detection of autoantibodies from a sample that bind to one or more isoforms of Glycoprotein 2 (GP2), comprising

- providing a sample of a subject exhibiting symptoms and/or suspecting of having said disorder,
- providing two or more isoforms of Glycoprotein 2 (GP2), wherein at least one of isoforms 1 and/or 2 and at least one of isoforms 3 and/or 4 are provided
- contacting said sample with said one or more isoforms,
- detecting autoantibodies that bind to said one or more of isoforms.

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2. claims: 5(completely); 7, 9-15(partially)

Method for the diagnosis of Celiac disease (CeD), wherein the presence of IgG and/or IgA autoantibodies from a sample of said subject that bind to isoforms 1 and/or 2 of GP2 (SEQ ID NO 1 and/or 2) indicates the presence of CeD.

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3. claims: 6, 8(completely); 7, 9-15(partially)

Method for the diagnosis of Crohn's disease (CD), wherein the presence of IgG and/or IgA autoantibodies from a sample of said subject that bind to isoforms 3 and/or 4 of GP2 (SEQ ID NO 3 and/or 4) indicates the presence of Crohn's disease

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**ANNEX TO THE EUROPEAN SEARCH REPORT  
ON EUROPEAN PATENT APPLICATION NO.**

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This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report.  
The members are as contained in the European Patent Office EDP file on  
The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

17-09-2015

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